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Spectroscopic studies of FixL, an O_2 sensing heme protein

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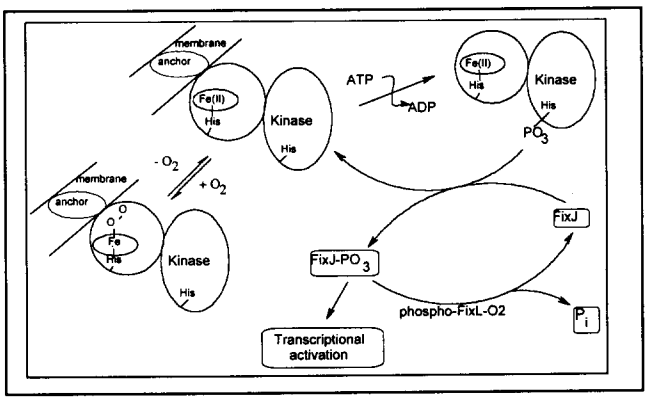
FixL is the sensor component of the bacterial two-component signal transduction system responsible for regulating N_2 fixation in several species of bacteria. FixL contains a heme domain capable of reversible O_2 binding and a kinase domain whose activity is inhibited in response to heme oxygenation. This inhibition results in failure to phosphorylate the response regulator, FixJ, leaving it transcriptionally inactive toward *nifA* and *fixK*. We are pursuing a molecular-level understanding of the mechanism by which FixL's kinase activity is coupled to binding or release of O_2 by the heme. Data from cw and time-resolved spectroscopic methods will be presented and interpreted in terms of a model for transmission of the signal between the heme and kinase domains of FixL.



N4Py iron complexes as model for iron bleomycin

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Iron-peroxo species are invoked in the mechanisms of a number of iron requiring biological oxidation catalysts. For example a low spin Fe(III)-OOH species has been characterized for "activated Bleomycin", the active form of the antitumor drug bleomycin (BLM). Activated BLM is formed by the reaction of Fe(II)-BLM with O_2 in the presence of a $1e^-$ reductant. The decomposition of this intermediate is thought to be responsible for the drug's ability to oxidatively cleave DNA. The accepted mechanistic proposal involves hydrogen abstraction by activated BLM at the C4' position of the deoxyribose unit of a nucleotide to form a C-4' carbon radical whose fate is determined by two subsequent pathways , one that requires additional O_2 and another that does not. Besides DNA cleavage activated BLM is also capable of oxidizing a wide variety of organic substrates.

In our efforts to gain a better understanding of the chemistry of iron Bleomycin we prepared a series of model complexes from the pentadentate ligand N4Py. Complexation of this ligand with iron(II) or iron(III) salts leads to the formation of a series of stable and well characterized complexes including $[(N4Py)Fe(CH_3CN)](ClO_4)_2$ (**1**), $[(N4Py)FeOMe]ClO_4)_2$ (**2**) and $[\{N4Py)Fe\}_2O](ClO_4)_2$ (**3**). Reaction of H_2O_2 lead to the formation of a transient purple species which has been spectroscopically (UV/Vis, EPR and ES-MS) characterized to be $[(N4Py)Fe(III)OOH]^{2+}$ (**4**). Resonance Raman spectroscopy showed the presence of weakened O-O bond. The purple intermediate **4** is formed from **1** in a two step process: first oxidation to give two iron(III) species, **2** and **3**, followed by an acid base reaction to give **4**. The reactivity of **1** in catalytic oxidations has been studied. A wide variety of organic substrates, including alkanes, alkenes, alcohols and aromatic substrates could be oxidized by **1**, using H_2O_2 as the oxidant. Monitoring the catalytic reactions with UV/Vis showed that **4** is involved in the catalytic reaction as the precursor for the active species. A possible mechanism for oxidations catalyzed by **1** will be discussed.